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#### **Abstract**

 $MINT: a \ multivariate \ integrative \ method \ to \ identify \ reproducible \ molecular \ signatures \ across \ independent \ experiments \ and \ platforms$ 

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#### 1 Datasets

- GSE74602
- GSE110223
- GSE110224

#### 1.1 Download

```
## $GSE74602
## ExpressionSet (storageMode: lockedEnvironment)
## assayData: 22184 features, 60 samples
## element names: exprs
## protocolData: none
## phenoData
    sampleNames: GSM1923670 GSM1923671 ... GSM1923729 (60 total)
    varLabels: title geo_accession ... tissue:ch1 (34 total)
    varMetadata: labelDescription
## featureData
   featureNames: ILMN_1343291 ILMN_1343292 ... ILMN_2038778 (22184 total)
    fvarLabels: ID Gene title ... Platform_SEQUENCE (22 total)
   fvarMetadata: Column Description labelDescription
## experimentData: use 'experimentData(object)'
## Annotation: GPL6104
## $GSE110223
## ExpressionSet (storageMode: lockedEnvironment)
## assayData: 22283 features, 26 samples
## element names: exprs
## protocolData: none
## phenoData
    sampleNames: GSM2982906 GSM2982907 ... GSM2982931 (26 total)
    varLabels: title geo_accession ... vb pet variable values:ch1 (64 total)
## varMetadata: labelDescription
## featureData
   featureNames: 1007_s_at 1053_at ... AFFX-TrpnX-M_at (22283 total)
   fvarLabels: ID Gene title ... GO:Component ID (21 total)
   fvarMetadata: Column Description labelDescription
## experimentData: use 'experimentData(object)'
    pubMedIds: 30809322
## Annotation: GPL96
##
## $GSE110224
## ExpressionSet (storageMode: lockedEnvironment)
## assayData: 54675 features, 34 samples
## element names: exprs
## protocolData: none
## phenoData
    sampleNames: GSM2982932 GSM2982933 ... GSM2982965 (34 total)
    varLabels: title geo_accession ... vb pet variable values:ch1 (63 total)
    varMetadata: labelDescription
## featureData
```

```
## featureNames: 1007_s_at 1053_at ... AFFX-TrpnX-M_at (54675 total)
## fvarLabels: ID Gene title ... GO:Component ID (21 total)
## fvarMetadata: Column Description labelDescription
## experimentData: use 'experimentData(object)'
## pubMedIds: 30809322
## Annotation: GPL570
```

### 1.2 Deleting Gene Symbols with no character or NAs

```
## $GSE74602
## ExpressionSet (storageMode: lockedEnvironment)
## assayData: 20498 features, 60 samples
## element names: exprs
## protocolData: none
## phenoData
   sampleNames: GSM1923670 GSM1923671 ... GSM1923729 (60 total)
    varLabels: title geo_accession ... tissue:ch1 (34 total)
    varMetadata: labelDescription
## featureData
   featureNames: ILMN_1343291 ILMN_1343292 ... ILMN_2038778 (20498 total)
## fvarLabels: ID Gene title ... Platform_SEQUENCE (22 total)
   fvarMetadata: Column Description labelDescription
## experimentData: use 'experimentData(object)'
## Annotation: GPL6104
##
## $GSE110223
## ExpressionSet (storageMode: lockedEnvironment)
## assayData: 21154 features, 26 samples
## element names: exprs
## protocolData: none
## phenoData
    sampleNames: GSM2982906 GSM2982907 ... GSM2982931 (26 total)
    varLabels: title geo_accession ... vb pet variable values:ch1 (64 total)
    varMetadata: labelDescription
## featureData
## featureNames: 1007_s_at 1053_at ... AFFX-HUMISGF3A/M97935_MB_at (21154 total)
   fvarLabels: ID Gene title ... GO:Component ID (21 total)
    fvarMetadata: Column Description labelDescription
## experimentData: use 'experimentData(object)'
    pubMedIds: 30809322
## Annotation: GPL96
## $GSE110224
## ExpressionSet (storageMode: lockedEnvironment)
## assayData: 45113 features, 34 samples
## element names: exprs
## protocolData: none
## phenoData
    sampleNames: GSM2982932 GSM2982933 ... GSM2982965 (34 total)
    varLabels: title geo_accession ... vb pet variable values:ch1 (63 total)
```

```
## varMetadata: labelDescription
## featureData
## featureNames: 1007_s_at 1053_at ... AFFX-HUMISGF3A/M97935_MB_at (45113 total)
## fvarLabels: ID Gene title ... GO:Component ID (21 total)
## fvarMetadata: Column Description labelDescription
## experimentData: use 'experimentData(object)'
## pubMedIds: 30809322
## Annotation: GPL570
```

### 1.3 All exprs into one list

```
## List of 3
## $ GSE74602 : num [1:20498, 1:60] 0.034 0.7627 0.5062 -0.0427 -0.0923 ...
## ... attr(*, "dimnames")=List of 2
## ... $ : chr [1:20498] "ILMN_1343291" "ILMN_1343292" "ILMN_1343293" "ILMN_1343294" ...
## ... $ : chr [1:60] "GSM1923670" "GSM1923671" "GSM1923672" "GSM1923673" ...
## $ GSE110223: num [1:21154, 1:26] 10.98 7.12 7.03 9.54 5.18 ...
## ... attr(*, "dimnames")=List of 2
## ... $ : chr [1:21154] "1007_s_at" "1053_at" "117_at" "121_at" ...
## ... $ : chr [1:26] "GSM2982906" "GSM2982907" "GSM2982908" "GSM2982909" ...
## $ GSE110224: num [1:45113, 1:34] 11.71 8.61 5.89 8.21 3.69 ...
## ... $ : chr [1:45113] "1007_s_at" "1053_at" "117_at" "121_at" ...
## ... $ : chr [1:45113] "1007_s_at" "1053_at" "117_at" "121_at" ...
## ... $ : chr [1:34] "GSM2982932" "GSM2982933" "GSM2982934" "GSM2982935" ...
```

#### 1.4 Annotation

```
## List of 3
## $ GSE74602 : num [1:20498, 1:60] 0.034 0.7627 0.5062 -0.0427 -0.0923 ...
## ... attr(*, "dimnames")=List of 2
## ... $ : chr [1:20498] "EEF1A1" "TUBB2A" "TXN" "ACTB" ...
## ... $ : chr [1:60] "GSM1923670" "GSM1923671" "GSM1923672" "GSM1923673" ...
## $ GSE110223: num [1:21154, 1:26] 10.98 7.12 7.03 9.54 5.18 ...
## ... attr(*, "dimnames")=List of 2
## ... $ : chr [1:21154] "MIR4640///DDR1" "RFC2" "HSPA6" "PAX8" ...
## ... $ : chr [1:26] "GSM2982906" "GSM2982907" "GSM2982908" "GSM2982909" ...
## $ GSE110224: num [1:45113, 1:34] 11.71 8.61 5.89 8.21 3.69 ...
## ... attr(*, "dimnames")=List of 2
## ... $ : chr [1:45113] "MIR4640///DDR1" "RFC2" "HSPA6" "PAX8" ...
## ... $ : chr [1:45113] "MIR4640///DDR1" "RFC2" "HSPA6" "PAX8" ...
## ... $ : chr [1:34] "GSM2982932" "GSM2982933" "GSM2982934" "GSM2982935" ...
```

### 1.5 Deleting probe ids with multiple gene id

```
## List of 3
## $ GSE74602 : num [1:20498, 1:60] 0.034 0.7627 0.5062 -0.0427 -0.0923 ...
## ..- attr(*, "dimnames")=List of 2
## ...$ : chr [1:20498] "EEF1A1" "TUBB2A" "TXN" "ACTB" ...
## ...$ : chr [1:60] "GSM1923670" "GSM1923671" "GSM1923672" "GSM1923673" ...
```

```
## $ GSE110223: num [1:19931, 1:26] 7.12 7.03 9.54 5.18 7.29 ...
## ..- attr(*, "dimnames")=List of 2
## ... $: chr [1:19931] "RFC2" "HSPA6" "PAX8" "GUCA1A" ...
## ... $: chr [1:26] "GSM2982906" "GSM2982907" "GSM2982908" "GSM2982909" ...
## $ GSE110224: num [1:42899, 1:34] 8.61 5.89 8.21 3.69 7.45 ...
## ... $: chr [1:42899] "RFC2" "HSPA6" "PAX8" "GUCA1A" ...
## ... $: chr [1:34] "GSM2982932" "GSM2982933" "GSM2982934" "GSM2982935" ...
```

### 1.6 Deleting Duplicated Gene Symbols

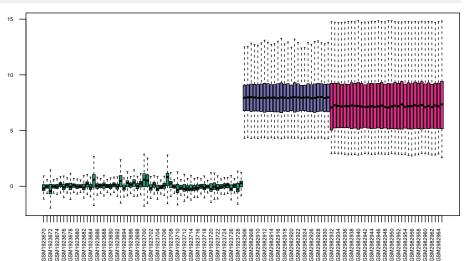
```
## List of 3
## $ GSE74602 : num [1:17181, 1:60] -0.4418 -0.3438 -0.0694 -0.3516 -0.5251 ...
## ... attr(*, "dimnames")=List of 2
## ... $ : chr [1:17181] "A1CF" "A2ML1" "A4GALT" "A4GNT" ...
## ... $ : chr [1:60] "GSM1923670" "GSM1923671" "GSM1923672" "GSM1923673" ...
## $ GSE110223: num [1:12500, 1:26] 10.28 7.77 6.38 9.44 8.34 ...
## ... attr(*, "dimnames")=List of 2
## ... $ : chr [1:12500] "A1CF" "A4GALT" "A4GNT" "AAAS" ...
## ... $ : chr [1:26] "GSM2982906" "GSM2982907" "GSM2982908" "GSM2982909" ...
## $ GSE110224: num [1:20844, 1:34] 5.14 10.24 4.69 3.92 5.7 ...
## ... attr(*, "dimnames")=List of 2
## ... $ : chr [1:20844] "A1BG-AS1" "A1CF" "A2M-AS1" "A2ML1" ...
## ... $ : chr [1:34] "GSM2982932" "GSM2982933" "GSM2982934" "GSM2982935" ...
```

#### 1.7 Concatenate

## 1.8 Grouping, Study and Tissue

## 1.9 raw boxplot

```
## pdf
## 2
```



```
## Healthy Tumor

## 60 60

## study

## Y GSE74602 GSE110223 GSE110224

## Healthy 30 13 17

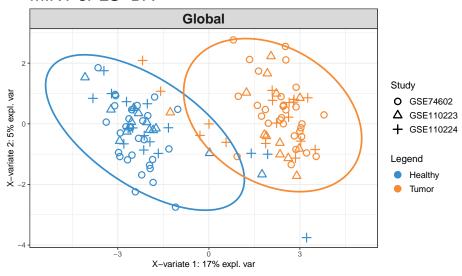
## Tumor 30 13 17
```

## 2.1 Selected Transcripts

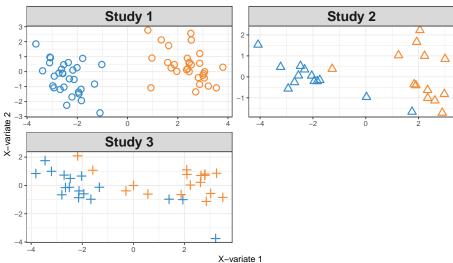
```
## $name
                         "TEAD4" "TMEM100" "BYSL" "ADH1B" "CEP55" "METTL7A"
## [1] "CDH3"
                "RERGL"
## [9] "KAT2B" "PPAT" "LRP8"
## $value
## value.var
## CDH3 0.53394033
          value.var
## RERGL -0.47491565
## TEAD4 0.38928441
## TMEM100 -0.38336054
## BYSL 0.32834300
## ADH1B -0.23884068
         0.10682962
## CEP55
## METTL7A -0.09615204
## KAT2B -0.06942520
## PPAT 0.02172650
        0.00717752
## LRP8
##
## $comp
## [1] 1
```

## 2.2 Sample Plot

### MINT sPLS-DA

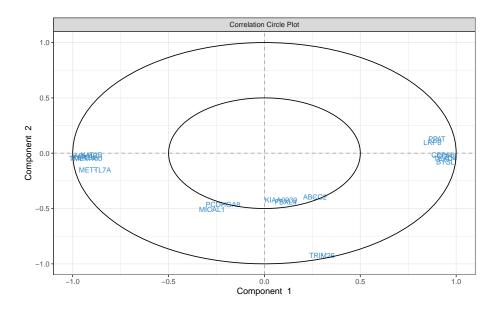


### MINT sPLS-DA

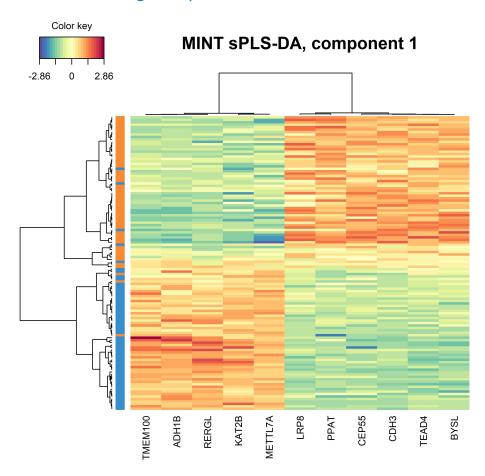


### 2.3 Correlation Circle Plot

highlights the contribution of each selected transcripts to each component (close to the large circle). See also more examples here.



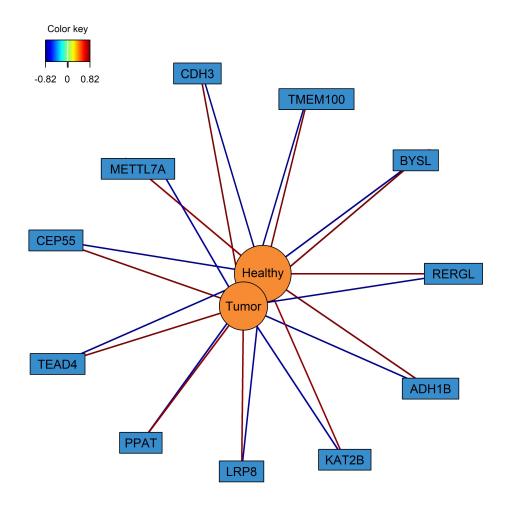
# 2.4 Clustered Image Map



More info about cim on this link.

### 2.5 Relevance Network

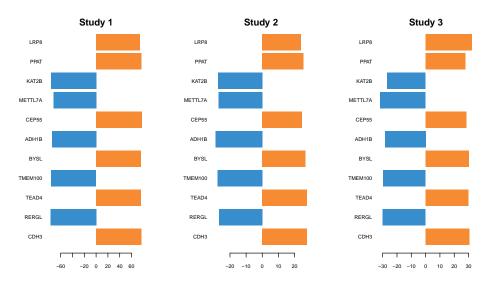
Relationship between the selected variables and the outcome of each category.



## 2.6 Loading Plot

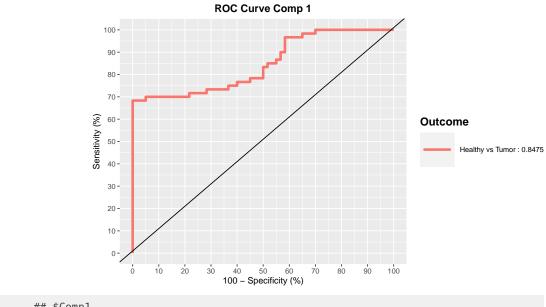
Displays the coefficient weight of each selected variable in each study and shows the agreement of the gene signature across studies. Colors indicate the class in which the mean expression value of each selected gene is maximal.

#### Contribution on comp 1



### 2.7 ROC

Area Under the Curve (AUC) and Receiver Operating Characteristic (ROC) curves for supervised classification.



## \$Comp1
## AUC p-value
## Healthy vs Tumor 0.8475 5.166e-11

# Session info

R version 4.0.5 (2021-03-31)

**Platform:** x86\_64-w64-mingw32/x64 (64-bit)

**locale:** LC\_COLLATE=English\_United States.1252, LC\_CTYPE=English\_United States.1252, LC\_MONETARY=English\_United States.1252, LC\_NUMERIC=C and LC\_TIME=English\_United States.1252

attached base packages: parallel, stats, graphics, grDevices, utils, datasets, methods and base

other attached packages: mixOmics(v.6.14.1), ggplot2(v.3.3.3), lattice(v.0.20-41), MASS(v.7.3-53.1), GEOquery(v.2.58.0), Biobase(v.2.50.0), BiocGenerics(v.0.36.1) and BiocStyle(v.2.18.1)

loaded via a namespace (and not attached): tidyselect(v.1.1.0), xfun(v.0.22), pander(v.0.6.3), reshape2(v.1.4.4), purrr(v.0.3.4), colorspace(v.2.0-0), vctrs(v.0.3.7), generics(v.0.1.0), htmltools(v.0.5.1.1), yaml(v.2.2.1), utf8(v.1.2.1), rlang(v.0.4.11), pillar(v.1.6.0), glue(v.1.4.2), withr(v.2.4.2), DBI(v.1.1.1), BiocParallel(v.1.24.1), RColorBrewer(v.1.1-2), plyr(v.1.8.6), matrixStats(v.0.58.0), lifecycle(v.1.0.0), stringr(v.1.4.0), munsell(v.0.5.0), gtable(v.0.3.0), evaluate(v.0.14), labeling(v.0.4.2), knitr(v.1.33), curl(v.4.3), fansi(v.0.4.2), rARPACK(v.0.11-0), Rcpp(v.1.0.6), readr(v.1.4.0), corpcor(v.1.6.9), scales(v.1.1.1), Bioc-Manager(v.1.30.12), limma(v.3.46.0), farver(v.2.1.0), RSpectra(v.0.16-0), gridExtra(v.2.3), ellipse(v.0.4.2), hms(v.1.0.0),digest(v.0.6.27), stringi(v.1.5.3), bookdown(v.0.22),dplyr(v.1.0.5), ggrepel(v.0.9.1), grid(v.4.0.5), cli(v.2.5.0), tools(v.4.0.5), magrittr(v.2.0.1), tibble(v.3.1.1), crayon(v.1.4.1), tidyr(v.1.1.3), pkgconfig(v.2.0.3), Matrix(v.1.2-18), ellipsis(v.0.3.1), xml2(v.1.3.2), assertthat(v.0.2.1), rmarkdown(v.2.7), rstudioapi(v.0.13), R6(v.2.5.0), igraph(v.1.2.6) and compiler(v.4.0.5)